

Remarks/Arguments

Claims 2, 5, 8 and 9 are pending in the application upon entry of the above claim amendments. Claims 1, 3, 4, 6, 7, and 10 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter in the canceled claims in a related application. Claims 2, 5, 8 and 9 have been amended. Support for the amendments to claims 2, 5, 8 and 9 can be found in the originally filed claims and throughout the specification.. No new matter has been added.

Rejections Under 35 U.S.C. § 101 Should Be Withdrawn

Claims 3 and 4 are rejected under 35 U.S.C. § 101 because the claims recite use without setting forth any steps involved in the process.

Claims 3-4 have been canceled without prejudice, which renders this rejection moot.

Rejections Under 35 U.S.C. § 112 Should Be Withdrawn

Claims 2-5 and 7-9 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner acknowledges that the specification teaches chemicals, such as compounds of formula I, which meet the written description and enablement provisions of 35 U.S.C. § 112. However, according to the Examiner, claims 2-5 and 7-9 are directed to encompass prodrug esters and derivatives which do not meet the written description requirement.

Applicants respectfully disagree. However, merely to expedite prosecution, the pending claims have been amended, which no longer encompass prodrug esters and derivatives. Thus, this rejection should be withdrawn.

Claims 1-5 and 7-10 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement for the treatment of cancers other than pancreatic and cervical cancers.

Applicants respectfully disagree. The test for enablement is whether one reasonably skilled in the art, following the teaching of the patent specification coupled with information known in the art at the time the patent application was filed, could make or use the invention without undue experimentation. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Field v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). It is not undue experimentation just because a considerable amount of experimentation need to be done, so long as the experimentation is merely routine or the specification provides reasonable amount of guidance and direction to the experimentation.

In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), and *In re Jackson*, 217 U.S.P.Q. 804, 807 (1982). Working examples are not necessary to meet enablement requirement, and lacking of examples should not be equated with lack of direction. "Nothing more than objective enablement is required, and therefore it is irrelevant whether the teaching is provided through broad terminology or illustrative examples." *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971).

The law does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. See *In re Fisher*, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970); see also, *In re Wright*, 27 U.S.P.Q.2d 1510 (Fed. Cir. 1993). To be enabled, all the law requires is that the scope of the enablement provided by the specification bear a "reasonable correlation" to the scope of the claims. *Id.* Moreover, even if evidence to doubt the proposed correlation exist, "the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q. 2d 1436, 1441 (Fed. Cir. 1995). A patent application, which contains a teaching of how to make and use the invention, must be taken as enabling unless there is reason to doubt the truth of the teachings. *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971).

The instant invention, as defined by the pending claims, requires a combination treatment using a matrix metalloproteinase inhibitor, a chemotherapy, and heat shock, that are not limited to one type of cancer. In light of the legal standard discussed above, Applicants submit that the claims, as amended, are enabled by the instant specification.

Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-4 have been canceled without prejudice, and this rejection is moot.

In view of the foregoing, Applicants respectfully request that the rejections under 35 U.S.C. § 112 be withdrawn.

Rejections Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 1-5 and 7-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Macpherson et al, WO 96/40101, (hereinafter "Macpherson"), in view of Evans et al, British J. of Cancer 85(12):1865-1870 (2001) (hereinafter "Evans"), further in view of Kouloulis et al., J. of Hepatobiliary Pancreatic Surgery 8:564-570 (2001) (hereinafter "Kouloulis").

Applicants respectfully disagree. To properly determine a *prima facie* case of obviousness, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P § 2142. This is important as "impermissible hindsight must be avoided

and the legal conclusion must be gleaned from the prior art.” *Id.* Four factual inquiries must be made: first, a determination of the scope and contents of the prior art; second, a determination of the differences between the prior art and the claims in issue; third, a determination of level of ordinary skill in the pertinent art; and fourth, an evaluation of evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). Three criteria may be helpful in determining whether claimed subject matter is obvious under 103 (a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int’l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex Inc. v. Ficoso N. Am. Corp.*, 299 F.3d 1313, 1333-1334 (Fed. Cir. 2002). The issue is whether there is apparent reason to combine (or to modify, in this case) the known elements in the fashion claimed by the patent at issue. *KSR Int’l Co. v. Teleflex, Inc.*

Macpherson teaches a specific matrix metalloproteinase inhibitor for treatment of cancer. Evans teaches that matrix metalloproteinase inhibitors are useful in the treatment of pancreatic cancer. Kouloulis teaches introoperative hyperthermia in combination with FU (5-fluoro-uracil) treatment. None of these prior arts teach or suggest a triple item treatment (*i.e.*, the obligatory use of an MMP-inhibitor, a chemotherapeutic, and heat shock), which is required by the instant claimed invention.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Claim Objections Should Be Withdrawn

The Examiner has objected the following claims: (1) claim 10 contains a typographical error, it appears that the claims intended to encompass “a matrix metalloproteinase inhibitor” where “inhibitor” was omitted; (2) claim 7 recites compounds disclosed in WO 98/14424 and other published patent applications, Applicants is required to amend the disclosure to include the material incorporated by reference.

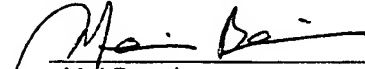
Claims 7 and 10 have been canceled, thus, the objections are moot.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner’s rejection and a notice of allowance are requested. If any issues remain in

connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Mei Benni', is written over a horizontal line.

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